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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,046	06/15/2006	Keiji Kubo	8279.1128USWO	7165

52835 7590 09/24/2009

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. BOX 2902
MINNEAPOLIS, MN 55402-0902

EXAMINER	
CHU, YONG LIANG	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
09/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,046	KUBO ET AL.	
	Examiner	Art Unit	
	YONG CHU	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,24-26 and 30* is/are pending in the application.

4a) Of the above claim(s) *14-26* is/are withdrawn from consideration.

5)☒ Claim(s) *18* is/are allowed.

6)☒ Claim(s) *1-17,19 and 30* is/are rejected.

7)☒ Claim(s) *1-17, 19, and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/13/2009 has been entered. Upon entering the submission, claims 1-19, 24-26, and 30 are pending in the instant application. Claim 18 has been allowed. Claims 24-26 remain withdrawn as non-elected subject matter.

Response to Arguments

Rejection under 35 U.S.C. § 112, 1st paragraph

Applicant's amendment obviates the instant rejection.

Rejection under 35 U.S.C. § 102(e)

Applicant's amendment obviates the instant rejection.

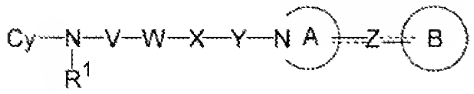
Since the amendment has overcome the rejections, the Examiner has expanded the search to part of the previously non-elected subject matter as disclosed follow, and new prior art renders the expanded scope of subject matter obvious:

Status of the Claims

Elected and Examined Subject Matter

The scope of the invention of the provisionally elected subject matter and the examined subject matter is as follows:

Applicants' claims are drawn to a compound of the formula (I)



, according to claim 1, wherein:

$\mathbf{C_y}$ is phenyl which may be substituted; $\mathbf{R^1}$ is a hydrogen atom; **V** is –C(O); **W** is $-NR^2$, wherein $\mathbf{R^2}$ is a hydrogen atom; **X** is a C_{1-4} alkylene, maybe substituted; **Y** is –C(O); **Z** is a bond or C_{1-6} alkylene maybe substituted; ring **A** is a piperidine or a piperazine ring, wherein both rings may be substituted; ring **B** is a piperazine ring, an imidazoline ring, an imidazole ring, a thiazoline ring or a fused nitrogen-containing heterocyclic ring which all the rings may be substituted, a pro-drug of the compound of claim 1, or a pharmaceutical composition comprising a compound thereof.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter of claims 1-17, 19, and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn compounds and compositions contain varying functional groups which are chemically recognized to differ in structure, function, and reactivity. The scope of the invention is set in considering the elected species and the preferred embodiments. In addition, a reference, which anticipates one group, would not render obvious the other.

Therefore, claims 1-19, and 30 (in part) will be examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, claims 2 and 30 are rejected due to claiming a prodrug of a compound of Formula (I). The instant specification defines "prodrug" of a compound of formula (I) according to claim 1 at paragraphs [156-157] as a compound that is converted to Compound (I) by a reaction induced by enzyme, gastric acid or the like under the physiological conditions in vivo, that is, a compound that is converted to Compound (I) by enzymatic oxidation, reduction, hydrolysis or the like, or a compound that is converted to Compound (I) by gastric acid-induced hydrolysis. According to Wikipedia, prodrugs can be classified into two types based on their sites of conversion into the final active drug form: Type I, those that are converted intracellularly (e.g., anti-viral nucleoside analogs, lipid-lowering statins, antibody-directed/gene-directed enzyme prodrugs [ADEP/GDEP] for chemotherapy), and Type II, those that are converted extracellularly, especially in digestive fluids or the

systemic circulation (e.g., etoposide phosphate, valganciclovir, fosamprenavir). Both types can be further categorized into subtype A or B, based on additional criteria. Those for the Type IA and IB are whether or not the cellular converting location is the site of therapeutic action. For the Type IIA and IIB, they are categorized depending on whether the conversion occurs in the gastrointestinal (GI) fluids or systemic circulation, *Wu and Farrelly, Toxicology 236:1-6, 2007*. However, such "prodrug" of the Formula (I) is not described in the specification to reasonably convey one skilled in the art, because each compound is different, and a prodrug of the compounds resulting from different metabolizing pathways lead to different compounds. Without disclosing a specific core structure of the prodrugs, it is impossible to carry out a comprehensive prior art search. Therefore, the specification fails to comply with the written description requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 recite the limitation "ring **B** is a monocyclic nitrogen containing heterocyclic ring and wherein the ring is a morpholine ring, .." in claim 1. However, there is no morpholine ring included in ring **B** according to the amended claim 1. There is insufficient antecedent basis for this limitation in the claim.

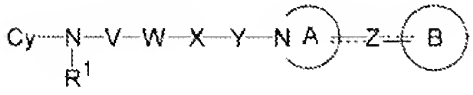
Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

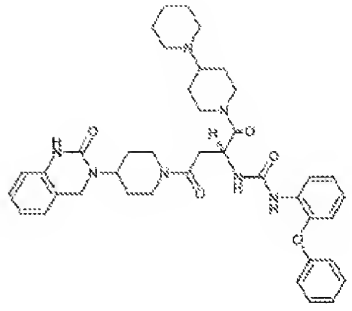
Claims 1, 3-8, 10, 12, 15, 17, and 19 are rejected under 35 U.S.C. 102 (b) as being anticipated by Chaturvedula et al., *WO03104236* ("the `236 publication"), published on 12/18/2003, and filed on 05/27/2003.

Applicants' claims are drawn to a compound of the formula (I)

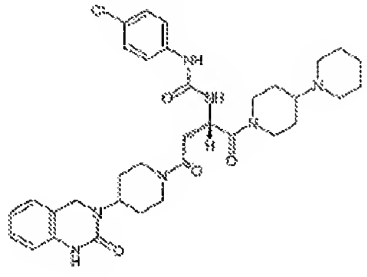


, according to claim 1, wherein:

$\mathbf{C_y}$ is phenyl which may be substituted; $\mathbf{R^1}$ is a hydrogen atom; **V** is –C(O); **W** is $-NR^2$, wherein $\mathbf{R^2}$ is a hydrogen atom; **X** is a C_{1-4} alkylene, maybe substituted; **Y** is –C(O); **Z** is a bond maybe substituted; ring **A** is a piperidine ring, wherein the ring may be substituted; ring **B** is a fused nitrogen-containing heterocyclic ring which the ring may be substituted, or a pharmaceutical composition comprising a compound thereof.



The `863 publication discloses specific compounds

as the compound 135 at page 135, and  as the compound 140 at page 136 of Table 3, and a pharmaceutical composition comprising a compound thereof. These compounds anticipate the instantly elected scope of invention.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

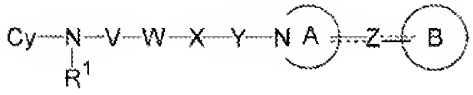
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-17, and 19 are rejected under 35 U.S.C. 103 (a) as unpatentable over the `863 publication.

Applicants' claims are drawn to a compound of the formula (I)

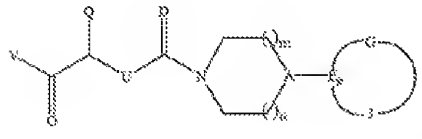


, according to claim 1, wherein:

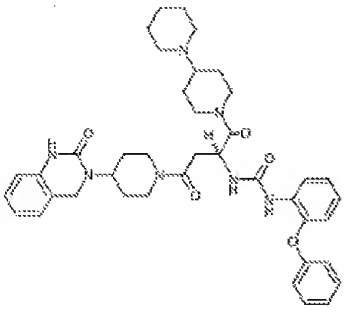
$\mathbf{C_y}$ is phenyl which may be substituted; $\mathbf{R^1}$ is a hydrogen atom; **V** is –C(O); **W** is $-NR^2$, wherein $\mathbf{R^2}$ is a hydrogen atom; **X** is a C_{1-4} alkylene, maybe substituted; **Y** is –C(O); **Z** is a bond or C_{1-6} alkylene maybe substituted; ring **A** is a piperidine or a piperazine ring, wherein both rings may be substituted; ring **B** is a piperazine ring, an imidazoline ring, an imidazole ring, a thiazoline ring or a fused nitrogen-containing heterocyclic ring which all the rings may be substituted, a pro-drug of the compound of claim 1, or a pharmaceutical composition comprising a compound thereof for treating inflammation.

Determination of the scope and content of the prior art (MPEP §2141.01)

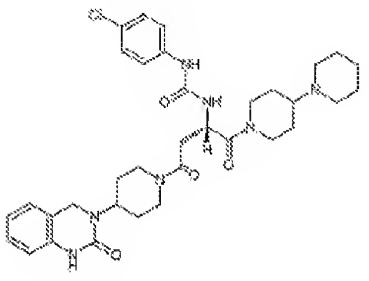
The `863 publication discloses a compound of the Formula (I)



, wherein **A** is C, or N; if p is 1, then G, J, and E together form $\mathbf{A^x}$ or $\mathbf{A^y}$, wherein $\mathbf{A^x}$ is a fused heterocycle having two fused rings, and $\mathbf{A^y}$ is a 4 to 6 membered heterocycle, according to claim 1, with specific examples of



compound 135 , and compound 140



as antagonists of CGRP-receptor for the treatment of inflammation.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the `863 compounds and the instantly claimed invention is that the substituent **X** is substituted ethylene for the prior art, while **X** is optionally substituted methylene for the instant invention.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

To those skilled in the medicinal chemistry art, the prior art teaching in the `863 publication renders the instantly claimed inventions obvious, because the difference between the prior art compounds and the instantly claimed compounds is the substituents **X** as ethyl vs. methyl linker. Both instant application and the prior art teach compounds can be used for a pharmaceutical application, namely treating inflammation. To those skilled in the chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists

knowing properties of one member of series would in general know what to expect in adjacent members, In re Wilder, 563 F.2d 457, 195USPQ 426 (CCPA 1977), and MPEP§2144.09. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e. pharmacological use). Therefore, the instantly claimed compounds would have been suggested to one skilled in the art.

Claim Objections

Claims 1-17, 19, and 30 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Conclusion

- Claim 18 is allowed.
- 1-17, 19, and 30 are rejected.
- 1-17, 19, and 30 are objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu, Ph.D., whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Status Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong Chu/
Patent Examiner
Art Unit 1626